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Comparative effects of education and bilingualism on the onset of mild cognitive impairment

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Abstract

Background: Increasing evidence suggests that life course factors such as education and bilingualism may have a protective role against dementia due to Alzheimer disease. This study aimed to compare the effects of education and bilingualism on the onset of cognitive decline at the stage of mild cognitive impairment (MCI). **Methods:** A total of 115 patients with MCI evaluated in a specialty memory clinic in Hyderabad, India, formed the cohort. MCI was diagnosed according to Petersen's criteria following clinical evaluation and brain imaging. Age at onset of MCI was compared between bilinguals and monolinguals, and across subjects with high and low levels of education, adjusting for possible confounding variables. **Results:** The bilingual MCI patients were found to have a clinical onset of cognitive complaints 7.4 years later than monolinguals (65.2 vs. 58.1 years; $p = 0.004$), while years of education was not associated with delayed onset (1--10 years of education, 59.1 years; 11--15 years of education, 62.6 years; >15 years of education, 62.2 years; $p = 0.426$). **Conclusion:** The effect of bilingualism is protective against cognitive decline, and lies along a continuum from normal to pathological states. In comparison, the role of years of education is less robust.

Introduction

Several life course variables including education, occupation, social networking, and bilingualism provide a reserve to cope better with the cognitive effects of aging and dementia [1--6]. While considerable evidence exists for the protective effect of education, mixed results have also been reported [5, 7]. This variability has been attributed to an interaction of education with other sociodemographic factors such as gender, rural residence, occupation, and cardiovascular risk factors [5, 8, 9]. Recent evidence indicates that bilingualism is also an important protective factor; the onset of Alzheimer disease (AD) was delayed by 4--4.5 years in bilinguals compared to monolinguals [2, 3, 10]. However, this effect has not always been replicated [11, 12].

The beneficial effects of both bilingualism and education have been linked to their effects on cognitive functions. Higher levels of education were associated with better performance in attention, working memory, conceptualization ability, calculation, and verbal fluency [13]. The current view of the advantage of bilingualism is that it is achieved through “permanent, intensive and versatile mental training” associated with constant use of more than one language [14]. It has been suggested that the interactional contexts bilinguals find themselves in (single language, dual language, and code-switching) lead them to adapt various cognitive control processes that result in efficient use of control networks [15]. Structural brain changes and reorganization of brain networks, which in turn sustain cognitive performance during aging, have also been demonstrated with both education and bilingualism [16--19].

A role of neurobiological markers in mediating cognitive reserve has recently been suggested. Lower concentrations of cerebrospinal fluid (CSF) $A\beta_{42}$ were demonstrated in mild cognitive impairment (MCI) patients with higher education who subsequently progressed to dementia compared to those with lower education [20]. A recent study on CSF biomarkers found that early bilingualism was associated with lower CSF total tau levels and a lower prevalence of preclinical AD [21].

However, this area remains complex and is a topic of ongoing debate, due to confounding effects of other sociodemographic factors, immigration, type of education, language use profile, methodological heterogeneity, and variable results [5, 11, 12, 22]. In a recent study from India, education was not independently associated with a

significant delay in onset of dementia, while bilingualism had a protective effect, after accounting for confounding sociodemographic factors [9].

It is well established that dementia is preceded by an early state of milder cognitive dysfunction, and that accumulation of AD-related pathology is already present in incipient AD [23]. The concept of MCI has been proposed to represent a cognitive continuum between normal aging and early AD [24]. Previous studies have provided supportive evidence for the protective role of cognitive reserve as measured by education and premorbid verbal IQ in MCI [20, 25]. Few studies have explored the protective effect of bilingualism in MCI [26, 27]. An older age at onset was demonstrated in bilinguals with amnesic MCI compared to monolinguals in a study by Ossher et al. [26]. However, the study participants were largely immigrants. Further, diagnoses were made based mainly on clinical examination. Brain imaging and investigations to exclude other causes such as vascular disease were not available.

To explore the association between MCI, education, and bilingualism further, this study was undertaken in a cohort of nonimmigrant subjects in and around Hyderabad, a place where bilingualism is common and part of everyday life. Monolingualism in this cohort was present in a smaller proportion of people living in areas in Hyderabad and other towns, where Telugu is the predominant language and Dakkhini-speaking minorities are few. This cohort also offers a particular opportunity to study the interaction between education and bilingualism [9]. Although overall, bilingualism in India is associated with higher education, languages are acquired not only at school but also in everyday social and working life, and it is not unusual to find bilinguals with low education. It is therefore possible to dissociate the two variables.

All subjects in the study were referred over a period of 8 years to the memory clinic of Nizam's Institute of Medical Sciences, a specialist service developed for systematically studying risk factors, clinical features, and outcomes of a cohort of patients with cognitive disorders [28, 29]. We aimed to compare the role of education and bilingualism on age at onset of MCI in the Indian context.

Subjects and Methods

Subjects

Consecutive subjects aged 45 years and above diagnosed with MCI in a specialist Memory Clinic in a university hospital in Hyderabad between June 2006 and December 2014 were included. We chose a younger age threshold than most other studies in the West, because memory clinic cohorts in developing countries like India are characterized by a higher proportion of early onset dementias (49.8%) [29]. This is related to younger demographics of population in India and higher cardiovascular risk burden, resulting in a higher frequency of early onset AD, Vascular dementia and Frontotemporal dementia. A later threshold of 60 or 65 years would miss many patients with early onset dementia, which might be even more sensitive to potential bilingualism effects. [30] All subjects were comprehensively evaluated clinically and with investigations including brain imaging, and the diagnosis of MCI was established by Peterson's criteria [24]. The subjects gave their informed consent, and the study was approved by the Institutional Ethics Committee of Nizam's Institute of Medical Sciences.

All subjects who complained of mild memory problems underwent detailed demographic, clinical and imaging profiling. Demographic and clinical details that include age at presentation, gender, age at onset of symptoms, education, mono vs bilingualism, occupation, rural vs. urban dwelling, history of stroke and the presence of vascular risk factors were recorded as per a standardized protocol [28,29]. Our cohort was grouped into those with 1-10 years of education which represents primary and secondary schooling, 11-15 years of education which constitutes under graduation, and more than

15 years of formal education which represents post graduation as per Indian educational system. Bilinguals in this study were defined based on Mohanty' s definition as those with an ability to meet the communicative demands of the self, and the society in their normal functioning in 2 or more languages in their interaction with the other speakers of any or all of these languages [31]. We realize that this definition might appear simplistic, as it does not take into account many important aspects of bilingualism, from grammatical competence to the mastery of reading and writing. However, its emphasis on the ability to communicate rather than abstract knowledge is in line with recent insights about the importance of actual language use in explaining potential bilingualism effects [32].

All participants were evaluated using the Addenbrooke's Cognitive Examination-Revised (ACE-R) or its later version Addenbrooke's Cognitive Examination-III (ACE-III) adapted into Telugu, Hindi, Indian English and Dakkhini for the Indian population, and the Clinical Dementia Rating (CDR) scale to ascertain severity of cognitive impairment [28, 33]. The ACE-III and the ACE-R assessed the patient's global cognition as well as performance in sub domains of memory, attention, fluency, language and visuospatial functions. Subjects with dementia, head injury, seizures, stroke, depression, anxiety and other psychiatric, neurological or medical disorders that may result in impaired cognition were excluded as per study protocol (Fig. 1). All patients underwent brain imaging and those with vascular changes that were likely to be the cause of cognitive impairment, that included strategically located infarcts and Fazekas grade II and III white matter hyper intensities were diagnosed as Vascular MCI and excluded [33].

Patients with abnormal thyroid functions and low vitamin B12 levels were also excluded.

Neuropsychological evaluation

Episodic memory of patients was evaluated using the Rey Auditory Verbal Learning Test- Delayed Recall (RAVLT-DR) and executive functioning using the verbal fluency score of ACE-R and ACE-III, Trail making test B (TMT – B) or Color Trails Test-B (CTT-B). Language was assessed on a 26-point composite score derived from the naming of 12 pictures, reading and writing, comprehension and repetition on items of the ACE-R and ACE-III. The Rey Osterrieth Complex Figure Test-copy (RCFT-Copy) and visuospatial domain score of ACE-R and ACE-III were used to assess visuospatial function. These tests have been validated in the Indian context with norms available for persons with varying levels of education, and are widely used in neuropsychological practice [28, 33, 34]. Furthermore, they have been found to be sensitive to early cognitive deficits [28]. Age, sex and education matched cutoff scores derived from the normative data were used to detect the cognitive impairment [28, 33, 34]. Since the study subjects were included during a period of eight years, the neuropsychological tests used in the clinic were variable across subjects and different versions of the test or different tests for individual cognitive domains were used. Subjects were considered to be impaired in the cognitive domains of memory, executive function, language and/or visuospatial functions, if their scores on these tests were found to be 1.5 SD lesser than the age, and education-matched normative data.

Diagnosis

Patients were diagnosed for MCI by experienced clinicians using the data derived from

the neuropsychological testing, imaging and clinical evaluation. The Peterson's criteria were used for the final diagnoses for MCI [24]. The patients were grouped into Amnestic MCI (impairment of memory with or without other cognitive domain impairment) and non- amnestic MCI (impairment of other cognitive domains except memory). Subjects who presented with memory complaints but showed no impairment on the neuropsychological tests were termed as Subjective Memory Impairment (SMI) and were excluded from the current cohort.

Statistical Analysis

The clinical and demographic profiles of monolingual and bilingual subjects were compared using chi Square and independent samples 't'test. The univariate general linear model (GLM) was done to assess the effect of education and bilingualism after adjusting for various demographic and clinical variables. Interaction effects of bilingualism with the various variables were also calculated by using univariate general linear model (GLM). Statistical analysis was performed using SPSS 20.0 for windows software (SPSS Inc., Chicago, IL). p value < 0.05 was considered significant.

Results

The study cohort constituted of 115 patients diagnosed as MCI whose mean age at presentation was found to be 63.8 years. 79.1% were diagnosed as amnestic MCI and 20.9% as non-amnestic MCI. The mean educational status was 14.5 years (SD 3.9 years, range 4-25 years); 23 subjects had 1 - 10 years of education, 47 had 11-15 years and 45 had more than 15 years of education. Of the 93 bilinguals (80.9%), 34 subjects

spoke two languages, 43 spoke 3 languages and 16 spoke 4 or more language combinations. 22 subjects spoke only one language.

To study the association of education with age at onset of MCI, we compared subjects with different levels of education; 1-10 years, 11-15 years and >15 years (Table-1).

There was no significant difference in age at onset between the three education groups. ($p=0.426$). Highly educated group (above 15 years of education) had better performance compared to school educated group on global cognitive assessment, verbal fluency and visuospatial functions (Table-2). We compared demographic, clinical and cognitive characteristics between monolingual and bilingual MCI subjects (Table-3). The mean age at onset of bilinguals was 63.2 years with a difference of 7.4 years, which was found to be significantly higher than that of monolinguals (55.8 vs 63.2 years, $p=0.004$).

Bilinguals also had a significantly higher age at presentation compared to monolinguals (58.1 vs. 65.2 years, $p=0.004$). Bilinguals were found to perform significantly better on global cognitive assessment, verbal fluency and visuospatial domains (Table-2).

Since MCI is a heterogeneous entity, we analyzed differences in age at onset between amnesic and non-amnesic MCI: bilinguals with amnesic MCI had a later age at onset compared to monolinguals (63.5 ± 9.5 years vs. 55.3 ± 11.7 , $p=0.005$), while this difference was not statistically significant in non- amnesic MCI (61.8 ± 13.1 years vs. 55.7 ± 13.8 , $p=0.387$).

As our bilingual cohort was more educated than monolinguals, we performed a subgroup analysis of an education- equivalent sample of monolinguals ($n=22$) and bilinguals ($n=30$) (10.4 vs 11.7 years of education, $p=0.107$) to analyze the effect of bilingualism without education as a potentially confounding factor. The mean age at

onset of bilinguals in this subgroup was significantly higher with a difference of 7.7 years, than that of monolinguals (55.8 vs 63.5 years, $p=0.015$).

Further, to assess the independent association of the different variables on age at onset, a univariate general linear model was performed. Bilingualism ($F_{1,113}=8.76$, $p=0.004$), vascular risk factors ($F_{1,113}=7.47$, $p=0.008$) and duration of illness ($F_{1,113}=7.26$, $p=0.019$) were found to have an independent association with age at onset, while education was not found to be independently associated with age at onset after adjusting for other variables such as gender, occupation, rural dwelling and ACE scores. Further, we looked for any interaction effects of other variables with bilingualism and found no interaction effects of gender ($F_{1,113}=1.09$, $p=0.30$), years of education ($F_{1,113}=0.05$, $p=0.82$), vascular risk factors ($F_{1,113}=0.004$, $p=0.98$), duration of illness ($F_{1,113}=2.38$, $p=0.13$), occupational status ($F_{2,112}=2.26$, $p=0.09$), rural/ urban dwelling ($F_{1,113}=2.57$, $p=0.11$), and ACE ($F_{1,113}=0.61$, $p=0.44$).

Discussion

Our study compares the influence of bilingualism and education on age at onset of MCI. While the age at onset in bilinguals was delayed by 7.4 years compared to monolinguals, no such delay was demonstrable in high educational groups. Furthermore, while the bilingualism-related delay reported in dementia is usually around 4-6 years, [2, 3, 10, 30] the difference in this cohort of MCI was much greater (7.4 years). This finding raises the possibility that bilingualism delays the onset of dementia but it might not affect disease progression.

In comparison, the effect of years of education on cognitive decline does not appear as robust. Both bilinguals and subjects with high educational status outperformed their counterparts with monolinguals and low education on ACE total score, visuospatial domain and in verbal fluency. These findings are consistent with previous studies [13, 21, 35]. However, although MCI subjects with higher education had higher cognitive test scores, this benefit did not appear to be sufficient to delay onset of memory complaints.

Our findings support previous observations from India suggesting that bilingualism has a stronger influence on delaying dementia than has years of education [9]. The reason for the differential effects of education and bilingualism in the Indian context could be that bilingualism is acquired early, widely practiced through life, and therefore might express its benefits even as age advances [36]. The protective effect of education has been explained in the context of how early life advantages due to schooling contribute to cognitive reserve [9]. It is possible that crucial lifestyle or biological factors that followed the period of formal schooling may have diminished a possible protective independent effect of education on MCI [9, 37].

The relationship between education, bilingualism and dementia/MCI might vary across countries and cultures. Firstly, unlike in many Western countries, low education in India is not automatically associated with social exclusion, deprivation and unemployment. Lack of high levels of education can, therefore, be compensated for by socially interactive lifestyle and complex occupations [9]. Secondly, since in many Western

countries acquisition of different languages happens predominantly through school education, the effects of education and bilingualism might be difficult to disentangle. Accordingly, some of the previously reported education effects could be in fact due to bilingualism [38].

An interesting finding was the absence of a significant difference in age at onset of bilinguals and monolinguals in non-amnestic MCI group in contrast to amnestic MCI. This is consistent with current understanding that amnestic MCI is more likely to be associated with AD compared to non-amnestic MCI and has a higher rate of progression to Alzheimer's dementia [39]. Non-amnestic MCI represents a mixed population with a heterogeneous range of underlying causes and the effect of bilingualism is therefore not likely to be uniform in this group. Some of the non-amnestic patients might develop towards Vascular Dementia and Fronto-temporal Dementia and in this group we would expect, based on the current literature, a substantial effect of bilingualism [30]. However, this could be outweighed by patients with other etiologies, in which bilingualism does not play a similar role: a question which can only be solved through a large study comparing different etiologies.

Our study has some limitations. Firstly, it is based on a hospital population in which monolinguals, illiterates and people with low education are underrepresented compared to what is found in the community, which could potentially have resulted in a selection bias. A study has, however, shown that clinic cohorts are more likely to progress to AD than community MCI cohorts [40]. There were also fewer women overall, and with

greater numbers of them with low education. This is a reflection of lower literacy and poor health seeking behaviours of women compared to men in India as reported earlier [28, 29].

All our patients were also evaluated comprehensively with hematological investigations and brain imaging to exclude other causes of MCI. Secondly, bilingualism was defined as a dichotomous variable and we did not explore the frequency of language use, mode of acquisition and proficiency in the subjects. However, previous studies found a significant correlation between subjective assessment of language ability and objective measures of language proficiency [41].

To conclude, our study provides additional evidence that bilingualism is associated with a delay in onset of cognitive decline in an elderly population at a stage of preclinical AD, while the impact of education was not significant. In the Indian context of educational, linguistic and cultural heterogeneity, where the practice of bilingualism is widely prevalent and low educated people are integrated into society, the profile of protective and risk factors appears to be different from other cohorts. Our results imply that different societies will have their own unique risk and protective factor patterns that will need to be addressed, to prioritize strategies to reduce burden of dementia.

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Legend(s)

Fig.1. Flow chart depicting the numbers of study subjects at the different levels of recruitment and exclusion, as well as the final number of study subjects. MCI, mild cognitive impairment

Table 1: Demographic and clinical characteristics of patients with MCI with different levels of education

	1–10 years of education (<i>n</i> = 23)	11–15 years of education (<i>n</i> = 47)	>15 years of education (<i>n</i> = 45)	<i>p</i> value
Age at presentation, years	61.3 (12.1)	64.6 (10.0)	64.3 (10.4)	0.445
Age at onset, years	59.1 (12.4)	62.6 (10.4)	62.2 (10.7)	0.426
Duration of illness, years	2.1 (2.0)	1.9 (1.8)	2.1 (1.7)	0.806
Male	14 (60.9%)	39 (83%)	39 (86.7%)	0.034
Urban residence	18 (78.3%)	39 (83%)	43 (95.6%)	0.077
Bilingual	10 (43.5%)	38 (80.9%)	45 (100%)	<0.0001
Occupation				<0.0001
Service worker	11 (47.8%)	18 (38.3%)	5 (11.1%)	
Associate professional	4 (17.4%)	5 (10.6%)	1 (2.2%)	
Professional	2 (8.7%)	19 (40.4%)	39 (86.7%)	
Housewife	6 (26.1%)	5 (10.6%)	0	
One or more vascular risk factors	12 (52.2%)	36 (76.6%)	32 (71.1%)	0.109
MCI type				
Amnestic	15 (65.2%)	40 (85.1%)	36 (80%)	0.794
Nonamnestic	8 (34.8%)	7 (14.9%)	9 (20%)	0.316
Values are presented as means (SD) or <i>n</i> (%). MCI, mild cognitive impairment				

Table 2. Performance of the mono- and bilinguals and the patients with different levels of education in cognitive tests

	Language			Education			
	monolingual (<i>n</i> = 22)	bilingual (<i>n</i> = 93)	<i>p</i> value	1–10 years of education (<i>n</i> = 23)	11–15 years of education (<i>n</i> = 47)	>15 years of education (<i>n</i> = 45)	<i>p</i> value
ACE-R/ACE-III	86.2 (5.6)	89.3 (3.9)	0.003	86.7 (4.9)	88.1 (4.4)	90.3 (3.7)	0.003
Attention and orientation	17.2 (1.2)	17.2 (1.1)	0.963	17.2 (1.2)	17.1 (1.1)	17.4 (1.0)	0.400
Memory	22.1 (2.4)	22.7 (2.7)	0.339	22.7 (2.6)	22.1 (2.8)	23.2 (2.4)	0.122
Fluency	7.8 (2.3)	9.0 (2.5)	0.044	7.6 (2.5)	8.8 (2.1)	9.4 (2.7)	0.014
Language	24.9 (1.5)	25.2 (1.04)	0.258	24.9 (1.3)	25.3 (1.1)	25.1 (1.2)	0.476
Visuospatial function	13.6 (2.4)	15.2 (1.3)	<0.0001	14.1 (2.3)	14.9 (1.4)	15.2 (1.4)	0.023
RAVLT-Delayed Recall ^a	6.1 (3.9)	5.9 (3.0)	0.803	5.9 (3.6)	5.9 (3.0)	5.9 (3.2)	0.995
Color Trails Test ^b	215.3 (108.7)	203.4 (75.7)	0.671	190.4 (54.3)	225.1 (102.1)	189.9 (57.7)	0.211

ACE-R/III, Addenbrooke's Cognitive Examination-Revised/III; RAVLT, Rey Auditory Verbal Learning Test. ^a Missing data: *n* = 10 (monolinguals, *n* = 4; bilinguals, *n* = 6; 1–10 years of education, *n* = 4; 11–15 years of education, *n* = 3; >15 years of education, *n* = 3). ^b Missing data: *n* = 20 (monolinguals, *n* = 5; bilinguals, *n* = 15; 1–10 years of education, *n* = 5; 11–15 years of education, *n* = 9; >15 years of education, *n* = 6).

Table 3. Demographic and clinical characteristics of the monolingual and bilingual patients with MCI

	Monolinguals (<i>n</i> = 22)	Bilinguals (<i>n</i> = 93)	<i>p</i> value
Age at presentation, years	58.1 (11.4)	65.2 (9.9)	0.004
Age at onset, years	55.8 (12.2)	63.2 (10.1)	0.004
Duration of illness, years	2.2 (1.9)	2.0 (1.8)	0.654
Male	18 (81.8%)	74 (79.6%)	0.510
Urban residence	17 (77.3%)	83 (90.2%)	0.294
Years of education	10.4 (3.7)	15.5 (3.3)	<0.0001
Occupation			<0.0001
Service worker	12 (54.5%)	22 (23.7%)	
Associate professional	5 (23.7%)	5 (5.4%)	
Professional	1 (4.5%)	59 (63.4%)	
Housewife	4 (18.2%)	7 (7.5%)	
One or more vascular risk factors	14 (63.6%)	66 (71.0%)	0.333
MCI type			
Amnestic	14 (63.6%)	77 (82.8%)	0.604
Nonamnestic	8 (36.4%)	16 (17.2%)	0.205

Values are presented as means (SD) or *n* (%). MCI, mild cognitive impairment.

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